ORIGINAL CONTRIBUTION

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Intracranial complications of rhinosinusitis. A review, typical imaging data and algorithm of management*

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SUMMARY

Statement of the problem: *Intracranial complications of acute bacterial sinusitis remain life-threatening. We aimed to study the current features of the condition - illustration, clinical presentations, risk factors, and define a management strategy.*

Method of study: *A retrospective study. Review of inpatients treated for meningoencephalitic infections related to sinusitis in a tertiary emergency care center between 1992 and 2005. Data retrieved on age, sex, signs at admission, bacterial findings, sinus involvement, intracranial complications and outcome. We analyzed the relation of bacterial infection to sinus involvement, initial signs of intracranial complications, and risk factors, and reviewed the literature to define a management strategy.*

Main results: *We retrieved 25 files. Intracranial complications related to sinusitis involved largely men between second and third decade. No risk factor was clearly identified. Frontal and sphenoid sinuses were the most common site involved. Diffuse headache or two-step evolution headache and altered mental status were strongly correlated with meningitis and brain abscess. Empyema was the most common complication. A management algorithm has been defined: computed tomography was early performed to diagnose intracranial collection, and was repeated after 48 h if the clinical course was not favorable. The sinus was always drained by the safest way. Sequelae occurred in 16% of patients. No death occurred with this treatment strategy.*

Principal conclusion: *Intracranial complications of acute sinusitis are exceptional but remain potentially severe and may lead to death. Early imaging data and aggressive management, associating sinus and brain drainage, as well as combined antibiotic therapy, can limit mortality and the incidence of sequelae.*

Key words: sinusitis, intracranial complications, combined treatment, sinus drainage, CT scan

INTRODUCTION

Acute rhinosinusitis is one of the most frequent infections of the upper respiratory tract. It affects one person in 8 per year [(1)]. Expert opinion is divided about the appropriate therapy. Recommendations range from prolonged antibiotic therapy against beta-lactamase-producing organisms to symptomatic treatment, probably because the outcome of bacterial rhinosinusitis is most often spontaneously favorable. Guidelines to restrict the use of antibiotics to cases related to bacterial infection have been recently released [(2)]. Indeed, the rate of bacterial resistance is increasing in the western world and is thought to be related to the common use of antibiotics for any acute rhinosinusitis or pharyngitis, viral infection being the most frequent etiology.

However, sinus infection may spread to the meningoencephalitic compartment, and subsequent morbidity should not be underestimated. Complications include cerebral sequelae, which can be disabling in 25% of cases [(3)] and may cause death in 10% [(4)]. The contrast between recommendations, which lead to a deflation in therapy on the one hand, and the severity of intracranial complications on the other hand is the basis of this work. The aim of this study was to 1) to illustrate common intracranial complications of sinusitis 2) identify possible risk factors, and 3) to review the literature and propose an algorithm for management.

MATERIALS AND METHODS

Study design

A retrospective study was based on the files of patients treated for meningoencephalitic infections related to rhinosinusitis in a tertiary emergency care center. Adult patients were admitted to 3 departments involved in head and neck conditions in our hospital: the Ear, Nose and Throat department, the Neurosurgery department and the Headache centre. Patient files between

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1992 and 2005 were included. Patient records were screened for the following abnormalities of the ICD-10-CM classification: **subdural abscess, extradural abscess, brain abscess, meningitis, cavernous sinus or other intracranial venous sinus thrombophlebitis, or osteomyelitis**. Among these, we selected only cases related to rhinosinusitis as evidenced by clinical examination and computed tomography (CT) scan. Cases related to invasive fungal rhinosinusitis were excluded, as were those of orbital cellulitis. Every patient was documented by CT scan, and magnetic resonance imaging (MRI) in most cases. For each case, age, sex, time between first symptoms and diagnosis, signs at admission, previous treatment, medical history, type of intracranial complication and sinus involved were recorded. Duration of treatment, type of sinus drainage and neurosurgical intervention, complications, after-effects and mortality were reported. We determined whether symptoms at clinical presentation or use of anti-inflammatory medications were associated with certain types of complications.

Literature review

A review of the literature was performed focused on articles and guidelines dealing with intracranial complications of sinusitis. A bibliographical search was executed in the following databases: Medline, Pubmed and Medscape. Occurrence, morbidity and mortality of intracranial complications with rhinosinusitis as well as an algorithm of management were the data listed for comparison with our results.

Statistical Analysis

Data are described with numbers and percentages. Univariate analysis for correlation between complications and symptoms and anti-inflammatory medications involved the chi-square Fisher's exact test and Pearson's r coefficients. A $p < 0.05$ was considered significant.

RESULTS

Epidemiology

We identified 25 patients over 13 years (5 women; mean age 35 ± 21 years), representing 2 patients per year, on average, with intracranial complications due to rhinosinusitis.

Frontal sinus was the sinus mainly involved (n=16), either related to anterior rhinosinusitis (n=12) or to pansinusitis (n=4). Isolated sphenoiditis occurred in 9 cases. No case was related to dental infection.

Signs at admission

Headache was the most common complaint (40%, 10 cases) - localized in 4 cases and diffuse in 6. Among the cases, biphasic progression was observed in 5 patients in whom focal headache became diffuse. In 2 cases, isolated diffuse headache was the single symptom that led to the diagnosis of intracranial complication. Fever was uncommon (16%, 4 cases). All cases but 2 showed central signs: altered mental status (32%, 6 cases), abducent nerve palsy (20%, 5 cases), hemiparesis (8%, 2 cases), seizures (8%, 2 cases), and other cranial nerve palsies (8%, 2 cases). Two cases presented with Pott's puffy tumor (8%) and one with nuchal rigidity (5%). The presence of rhinologic signs such as rhinorrhea and nasal obstruction was not always documented in patient files.

Intracranial complications

The most frequent complication was sphenoid osteomyelitis (Table 1; Figure 2), followed by subdural empyema (Figure 3), related to frontal sinusitis. Six patients had several complications at the same time. One case of extradural empyema was localized to the planum sphenoidale (Figure 4), associated with acute sphenoiditis, without obvious bone lysis. Two cases of meningitis were related to sphenoiditis, with a bony dehiscence of the clivus in one case. The congenital or acquired origin of this dehiscence could not be demonstrated. A third case of meningitis was associated with sphenoiditis and cavernous sinus thrombosis (Figure 5). We also uncovered one case of sagittal superior sinus thrombosis (Figure 6) occurring with subdural empyema and brain abscess (Figure 7), complicating frontal sinusitis.

Clinical signs were tested for their association with intracranial complication. Diffuse headache (p=0.0043) and also altered mental status (p=0.0087) were significantly associated with meningitis. Altered mental status was also associated with brain abscess (p=0.0087). Fever was not predictive of osteomyelitis or abscess but was close to significance when associated to meningitis (p=0.061) or to brain abscess (p=0.056).

Table 1. Occurrence of intracranial complications in 25 patients with ABRS.

Complications	**No. of patients (%) (n=25)**
Sphenoid osteomyelitis	5 (20%)
Extradural empyema	4 (16%)
Subdural empyema	4 (16%)
Cavernous sinus thrombophlebitis	4 (16%)
Meningitis	3 (12%)
Brain abscess (Figure 7)	3 (12%)
Frontal bone osteitis	2 (8%)
Superior sagittal sinus thrombophlebitis (Figure 6)	1 (4%)
Multiple complications	6 (24%)

Table 2. Identification of bacterial samples.

Bacteria	**No. of Patients (%) (n=23)**	**Sinus**
Unidentified bacteria	11 (48%)	
Streptococcus intermedius	2 (9%)	Frontal
Streptococcus anginosus	1 (4%)	Frontal
Staphylococcus aureus	5 (22%)	4 sphenoid; 1 frontal
Streptococcus pneumoniae	1 (4%)	Sphenoid
Haemophilus influenza	1 (4%)	Sphenoid
Anaerobic streptococci	1 (4%)	Frontal
Aero-anaerobic bacteria	1 (4%)	Frontal sinus

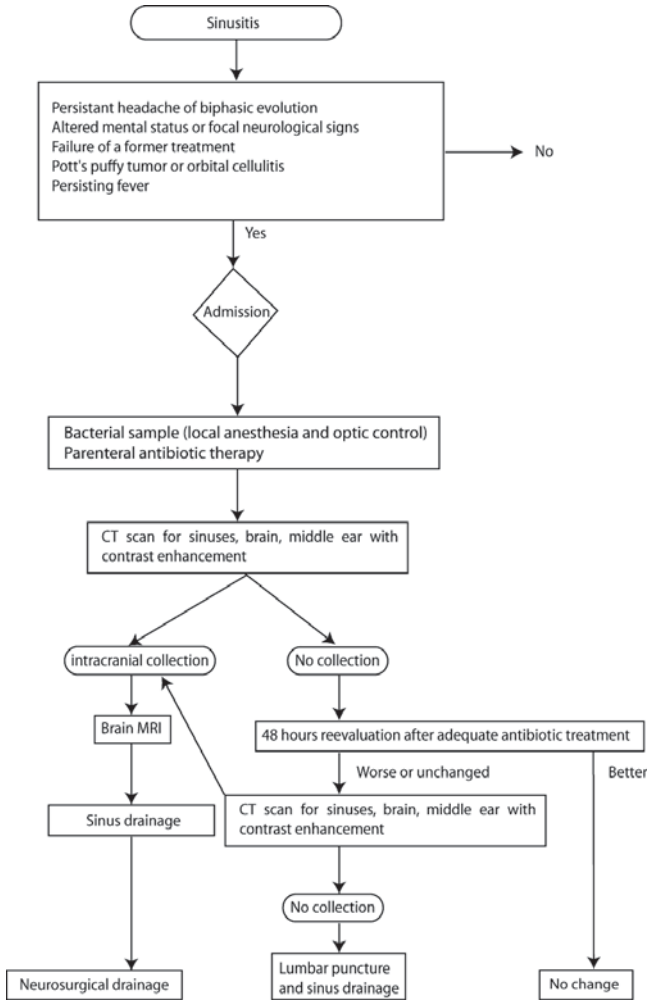

Figure 1. Algorithm for management for intracranial complications with acute bacterial rhinosinusitis (ABRS).

Figure 2. Sphenoid osteomyelitis. Spread of infection through the bone is attested by the presence of gas bullae in the left cavernous sinus.

Figure 3. Subdural empyema on the left fronto-parietal convexity. The subdural collection repulses midline structures.

Figure 4. Extradural empyema of the planum sphenoidale.

Figure 5. Cavernous sinus thrombosis. Notice the heterogeneous contrast enhancement of the left cavernous sinus.

Figure 6. Sagittal superior sinus thrombosis. On this lateral brain venogram, contrast enhancement is interrupted in the superior sagittal sinus.

Bacteriology

All patients but 2 had bacteriological analysis from surgical sinus sampling (Table 3). Twelve specimens provided bacterial identification. *Staphylococcus aureus* was predominantly found in the sphenoid sinus. In the frontal sinus, *Streptococcus* from the intermedius group, together with anaerobic bacteria, were most commonly retrieved.

Natural history

In a few cases, infective rhinosinusitis was discovered because of the onset of an intracranial complication without preceding symptoms. In 12 cases, rhinologic symptoms were present for less than 2 weeks.

Figure 7. Extradural empyema and abscess of the frontal lobe with brain oedema.

Nine patients were treated for rhinosinusitis before being referred to hospital. Among them, seven were given antibiotics according to current guidelines. In 2 cases, patients received only corticosteroids without antibiotics. Only 2 patients received non-steroidal anti-inflammatory drugs.

Nonparametric analysis failed to establish any significant relation between nonsteroidal anti-inflammatory or steroidal drug use and each intracranial complication.

IDENTIFICATION OF RISK FACTORS

Comorbidity

None of the patients included in this series was treated for chronic sinusitis, and only 1 case for diabetes mellitus.

Treatment modalities

Empiric treatment was begun for all patients, with a combination of intravenous third-generation cephalosporin, fosfomycine and metronidazole. Antibiotic therapy was secondarily adjusted according to bacteriological data. Heparin was prescribed for intracranial venous sinus thrombophlebitis. All cases involved had sinus drainage: endoscopic transnasal sphenoidotomy for sphenoid sinusitis and trephination by external approach for frontal sinusitis.

Intracranial abscesses were evacuated neurosurgically in most instances. However, in 2 cases, limited extradural abscess was monitored with repeat CT, and medical treatment resulted in disappearance of these collections.

Table 3. Occurrence of sequelae in 25 patients with intracranial complications due to sinusitis.

Sequelae	No. of patients
Hemiparesis	2
Frontal syndrome or superior function impairment	2
Inability to speak	1
Epilepsy	1
Blindness	1
Multiple sequelae	4

Sinus surgery and neurosurgery, if indicated, were always performed in the same time.

Functional endoscopic sinus surgery was performed in 3 cases, several months after initial treatment, because of persistent frontal sinusitis. In two cases of frontal osteomyelitis, progression of disease required frontal bone resection.

Morbidity and mortality

No death was reported in our series. Progression of the disease was observed in 2 instances, frontal osteomyelitis and intracranial venous sinus thrombophlebitis.

In the single case of longitudinal sinus thrombophlebitis, extensive osteomyelitis required frontal bone removal. Despite aggressive medical and surgical treatment, the patient experienced motor deficit related to bilateral subdural abscess, with frontal brain infarct on the left side. The patient eventually recovered, with residual minor motor deficit of the right hand. In the single case of bilateral cavernous sinus thrombophlebitis, bilateral ophthalmoplegia was followed by cervical cellulitis, which was treated conservatively. A few days later, altered mental status revealed a small cerebellar infarct on the left side, with palsy of the X and XII cranial nerves.

Isolated oculomotor palsies, present in 5 cases, resolved within 2 to 3 months, as did complete oculomotor palsy in the case of the female patient with bilateral cavernous sinus thrombophlebitis.

Sequelae

Sequelae occurred in 4 patients (16%), who presented with frontal sinusitis with subdural empyema (n=2) or frontal abscess (n=1), and with sphenoiditis (n=1). A list of these is given in Table 3.

REVIEW OF THE LITERATURE

The occurrence of intracranial complication is given in Table 4. Subdural empyema is the most frequent complication (14) reported (33% [22%-45%]), followed by brain abscess (27% [19%-35%]) and meningitis (20% [15%-26%]). Whereas complete recovery can be expected in the majority of cases (71% [61%-81%]) fatalities can be occur in 6% (3-9%) of cases of intracranial complication with bacterial rhinosinusitis. The mean incidence of sequelae is 23%. CT scan with contrast is the benchmark for the detection and diagnosis of intracranial complications and is recommended to be performed as early as possible whenever an intracranial complication can be suspected [6].

DISCUSSION

This study emphasizes the severity of acute bacterial rhinosinusitis(ABRS)-associated intracranial complications. The incidence of such complications has declined in the last half-century in developed countries [5-7]. Bradley et al., in a retrospective review from 1950 to 1980, found a four-fold decrease in the incidence of brain abscess secondary to ABRS [5], a

Table 4. Occurrence of intracranial complications with ABRS reported in the literature.

Series	n	Subdural empyema	Brain abcess	Extradural empyema	Meningitis	Cavernosus sinus thrombosis	Superior saggital sinus thrombosis	Osteomyelitis	Multiple
Singh (1995)	219	58%	17%	8%	10%				7%
Clayman (1991)	24	8%	46%		29%	8%	4%	4%	
Younis (2001)	39	13%	10%	18%	54%				
Altman (1997)	7							42%	71%
Jones 1995	12	33%	17%	25%		8%			8%
Sable 1984	16	88%	13%		6%			6%	13%
Gallagher (1998)	15	18%	14%	23%	18%	9%	9%	9%	
Bradley (1984)	54	48%	37%	6%					9%
Albu (2001)	16	25%	38%	31%	38%	13%			
Marshall (2000)	7	14%		14%				100%	29%
Giannoni (1997)	12	33%	42%	42%	42%				
Giannoni (1998)	10	40%	50%	20%	30%				40%
Jones (2002)	47	38%	30%	23%	2%	2%			
Present series	25	16%	12%	16%	12%	16%	4%	20%	24%
Mean		**33,23%**	**27,17%**	**20,55%**	**24,10%**	**9,33%**	**5,67%**	**30,17%**	**25,29%**
Standard deviation		**21,33%**	**14,21%**	**9,73%**	**16,32%**	**4,38%**	**2,36%**	**33,76%**	**22,16%**
95% Confidence interval		**[22%; 45%]**	**[19%; 35%]**	**[15%; 26%]**	**[14%; 34%]**	**[6%; 13%]**	**[3%; 8%]**	**[3%; 57%]**	**[11%; 33%]**

Table 5. Morbidity and mortality due to intracranial complications with ABRS reported in the literature.

Series	n	Complete recovery	Morbidity	Death
Beckhuis et Taylor (1969)			31%	
Hoyt et Fischer (1991)	9			14%
Jones (1995)	12	50%	42%	8%
Singh (1995)	219	38%	46%	16%
Giannoni (1997)	12	75%	25%	0
Giannoni (1998)	10	70%	20%	10%
Gallagher (1998)	15	80%	13%	7%
Marshall (2000)	7	100%	0	0
Lang (2001)	10	80%	20%	0
Younis (2001)	39	67%	10%	5%
Albu (2001)	16	69%	25%	6%
Jones (2002)	47	79%	19%	2%
Mean		**71%**	**23%**	**6%**
Standard deviation		**16,23%**	**12,77%**	**5,31%**
95% confidence interval		**[61%; 81%]**	**[15%; 30%]**	**[3%; 9%]**

progress which may be attributed to the increase of antibiotics use, and the use of CT scan [3, 5-15].

CT allows for early diagnosis of "high-risk" rhiosinusitis such as frontal sinusitis or sphenoiditis. Indeed, the sphenoid sinus is one of the main sources of intracranial complications. As evidenced in this series, many cases of sphenoiditis fail to present with rhinologic signs. Headache in these cases is the only symptom, and clinical diagnosis is challenging. In the present work, such cases were diagnosed and admitted through the Headache centre, whose procedures include undertaking CT for "unusual headache" [16]. In the absence of these imaging data, a diagnosis could be missed, and patients might receive symptomatic or even adverse treatment, which was the case for the patient with bilateral cavernous sinus thrombosis.

Type of complications

In the literature, subdural empyema is the most frequent complication [14] (Table 4): 33% [22%-45%], followed by brain abscess (27%) and meningitis (20%). Actually, early papers could not report on osteomyelitis, because of poor imaging data. In the present series, osteomyelitis was the most frequent complication, followed by empyema and brain abscess (Table 1). Multiple complications were observed in up to 25% of the cases.

Pathophysiology of spread of infection to intracranial spaces

Two-thirds of our cases were related to frontal sinusitis versus one-third to sphenoiditis [3,6-10,12,13,15,17,18]. The question of the precise origin of a complication is obviously difficult when the infection is diffuse, which may contribute to the variability of data reported in Table 5.

The history of the patients described herein strongly support the theory of venous spread of the infection. This corresponds to septic thrombophlebitis, developed in the sinus submucosal venous net, converging through Breschet veins, into the frontal bone diploe [6,11,12]. These veins are valveless, cross anterior and posterior cortical walls of the frontal sinus and converge on the meningeal veins. Thus frontal sinusitis can generate osteomyelitis, extradural or subdural abscess and even longitudinal sinus thrombophlebitis. This mechanism also accounts for the spread of infection from the sphenoid to the cavernous sinus. Arterial embolism, also possible [6,19-21], was unlikely in this series because of systematic proximity of the intracranial complication with the sinus.

A plea for early detection of complication

Diagnosis of a sinus-related complication may be challenging: complications might be asymptomatic in 15% of cases [12] or produce nonspecific symptoms, related to intracranial hypertension. Therefore, physicians should be aware of the putative morbidity of the disease and search for symptoms or signs suggestive of unfavourable outcomes such as relapsing headache [6,8].

Most of our patients had neither significant medical history nor specific predisposition to intracranial complications. Furthermore we found no patient with prior evidence of chronic rhinosinusitis or CT scan signs suggestive of chronic infection. Indeed the literature review did not clearly identify risk factors [3,7,8,12,22,23], except for the series of Clayman which reported 42% patients with diabetes mellitus or chronic renal failure [10].

As EPOS document [6], we advocate extensive use of CT for the diagnosis of intracranial complications arising from rhinosinusitis in cases of persistent headache ($p=0.0043$) of biphasic presentation, altered mental status ($p=0.0087$) or obviously if focal neurological signs or fever are present. Based on the review of the literature [6,7,11,24,25] and our experience, an algorithm of management is proposed in Figure 1.

Concomitant treatment of sinus and intracranial disease improves prognosis

Concomitant treatment of sinus and intracranial disease is the cornerstone of treatment [3,5-7,10,13,14,26], and should be performed as an emergency to avoid repeated surgical procedures due to ongoing intracranial infection. This point is made clear by the series of Jones, where repeated craniotomies were required only in the group of patients without initial sinus drainage [13].

First line sinus treatment was basic drainage (trephination or sphenoidotomy) which proved to be effective, and not extended endoscopic sinus surgery which might expose patients to bleeding, synechia or complications, which may in turn warrant another procedure as in the series of Fenton [22].

While sinus drainage should never be delayed, some cases of limited extradural brain abscess may be managed conservatively under neurosurgical supervision.

Morbidity and mortality

As illustrated in Table 5, the mean incidence of sequelae is 23% in the literature. Our results (Table 3) fit in that range.

The mean mortality rate reported in the literature is approximately 6%. We did not report any death, a result that may support our management strategy. However, Singh et al. described meningitis as the most dangerous complication [15], and it must be pointed out that few cases of meningitis were included in this series.

CONCLUSION

Intracranial complications of ABRS are rare but remain potentially severe. No risk factor has been clearly identified. Complications seem to be related to venous thrombosis, which allows for spread of infection. Early diagnosis with CT and immediate surgical procedure including sinus and brain drainage are mandatory, combined with antibiotic therapy, to prevent a fatal course and avoid sequelae.

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